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Preparation of Phosphinated Polymer-Incarcerated Palladium and Its Application to C–N and C–C Bond-Forming Reactions

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Abstract: Phosphinated polymer-incarcerated (PI) Pd catalysts were prepared by immobilization of palladium with phosphinated polymers by using the PI method. The phosphinated PI Pd catalysts showed good catalytic activity without externally added phosphine ligands in the amination of aryl halides for C–N bond-forming reactions, as well as in Suzuki–Miyaura and Sonogashira coupling. No leaching of palladium from the immobilized Pd was observed by fluorescence X-ray analysis. Furthermore, it was found that immobilization of Pd by the PI process facilitated the suppression of poisoning of the metal by amines. These effects can be ascribed to stabilization of the catalyst by both the phosphine moieties and the benzene rings in the swollen polymer support. The phosphinated PI Pd catalysts could also be recovered by simple filtration and reused several times without leaching of palladium in both the amination and Suzuki–Miyaura coupling reactions.

Keywords: amination · coupling reactions · heterogeneous catalysis · immobilization · palladium

Introduction

Palladium catalysts are useful and powerful tools for C–C and C–heteroatom bond-forming coupling reactions in organic synthesis. For example, C–C bond formation by Suzuki–Miyaura coupling, the Heck reaction, and Sonogashira coupling as well as amination or allylic substitution is widely used not only in the laboratory but also in industrial-scale reactions. In industry, however, contamination of the final products by leached metal residues is a serious problem and often precludes the application of palladium catalysts in these situations. One method aimed at obviating these problems involves the immobilization of the metal on a solid support. The immobilization of palladium in this way is attractive for a number of reasons. First, it facilitates easy separation and recovery of the catalyst from the reactants and products by simple filtration. This offers economic and environmental benefits as recovery and reuse of a heterogeneous catalyst decreases the amount of catalyst required and lowers the amount of metallic waste generated during the reaction. Second, immobilized catalysts are frequently heat-resistant or protect metals from oxygen or moisture in air, although this sometimes comes at the cost of lower catalytic activity than non-immobilized homogeneous catalysts. Lastly, immobilization avoids leaching of the metal, which often occurs under harsh amination conditions or with strong bases or polar solvents at the high temperatures commonly required for typical palladium-mediated reactions. In general, however, suppression of palladium leaching[1] conflicts with sustaining of catalytic activity, as strong immobilization of palladium atoms on a support limits the coordinative flexibility around palladium. Additives such as phosphine ligands enhance the catalytic activity[2] or selectivity in heterogeneous systems,[3] although leaching of palladium during reaction or on workup is still often observed. Furthermore, most of those additives are not recoverable and must be added again to the system at every cycle. Therefore, a simple catalyst system that does not require the external supply of phosphine ligands is desirable from both economic and operational standpoints.

To lower the influence of the leaching of phosphine ligands, palladium-immobilized heterogeneous catalysts with phosphinated polymer supports were investigated. In an early report, Trost and Keinan described polymer-supported palladium catalysts with diphenylphosphanyl groups on the surface of polystyrene resin.[4a] Following this, a variety of examples of phosphinated polymer-supported palladium cat-

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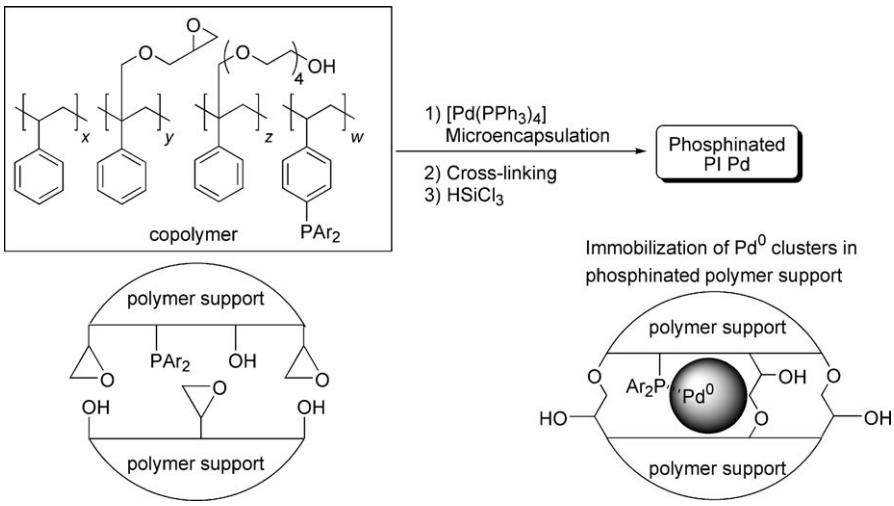
alysts were reported.[4b–o] Recently, we reported the immobilization of palladium clusters on polystyrene-based copolymers by using the polymer-incarcerated (PI) method.[5,6] These heterogeneous phosphinated PI Pd catalysts are highly active in C–C bond-forming reactions such as Suzuki–Miyaura coupling, the Heck reaction, or allylic substitution.[7,8] Furthermore, these catalysts were recovered quantitatively by simple filtration and reused several times without loss of activity. However, these PI Pd catalysts need externally added phosphine ligands to accelerate reactions, because the support on which the palladium clusters are immobilized is a non-phosphinated polymer. Therefore, to expand the varieties of coupling reactions that can be applied, some of which require more-demanding reaction conditions, it is desirable that phosphine moieties are incorporated into polymer supports to suppress leaching of palladium or phosphine.

The phosphine moiety of polymer supports[9] is assumed to have two main roles: 1) suppression of the leaching of palladium and 2) enhancement of catalytic activity as ligands. Therefore, it is expected that the introduction of phosphine moieties onto the polymer supports of PI Pd catalysts, instead of the external addition of the phosphine ligands, could be effective for accelerating oxidative addition. Phosphinated PI Pd catalysts have a mode of metal immobilization different to that of more-conventional phosphine-containing heterogeneous catalysts. The latter contain phosphine moieties only on the surface of the resin, which is already cross-linked before the immobilization of metals. However, the palladium clusters in PI Pd catalysts are immobilized not on the surface of the insoluble polymer but on the inside of the polymer support, and are held in place by the electrical and steric stabilization of both benzene rings[10] and phosphines[11] (Scheme 1). Phosphinated PI Pd catalysts can be prepared from polystyrene-based copolymers with phosphine moieties by using the PI method, just as with non-phosphinated PI Pd catalysts.



Scheme 1. Phosphinated PI Pd catalysts.

We reported that these heterogeneous phosphinated PI Pd catalysts are highly active for carbon–carbon bond-forming reactions such as Suzuki–Miyaura coupling[5f] even in the absence of externally added phosphine ligands. We also reported the chemoselective semi-hydrogenation of alkynes[5i] catalyzed by phosphinated PI Pd catalysts with phosphine moieties for partial catalyst poisoning. In semi-hydrogenation, there is a possibility that the phosphines in the polymer support may act as a weak poisoning agent of the metal, thus realizing both chemoselective hydrogenation and suppression of metal leaching.

Herein, we describe the preparation of PI Pd catalysts that contain phosphine moieties on the polymer supports and their application to several types of coupling reactions such as Suzuki–Miyaura coupling, amination of aryl halides, and Sonogashira coupling without addition of external phosphine ligands.

Results and Discussion

Preparation of Phosphinated PI Pd Catalysts

PI Pd catalysts **2a–j** were prepared from copolymer **1a–j** and $[Pd(PPh_3)_4]$, respectively, by the PI method (microencapsulation and cross-linking of polymer chains) described in our previous reports (Scheme 2 and Table 1). For comparison, we prepared non-phosphinated PI Pd catalyst **2j** without treatment of $HSiCl_3$ from the same type of polymer support without phosphine moieties. As some phosphines were oxidized to the corresponding phosphine oxides during the preparation of the catalyst, $HSiCl_3$ reduction gave phosphinated PI Pd catalysts. It was revealed by ^{31}P SR-MAS (swollen-resin magic-angle spinning) NMR spectroscopy[12] that the phosphine oxides on the copolymer were completely reduced to the corresponding phosphines.

Four equivalents of triphenylphosphine from $[Pd(PPh_3)_4]$ were eliminated during the immobilization and recovered as the oxide from the filtrate after washing (THF and hexane). The PI Pd catalysts **2a–j** thus prepared were then analyzed by transmission electron microscopy (TEM). TEM analysis of **2a** and **2f** (Figure 1) revealed that small Pd clusters were dispersed on the polymer support and that no large Pd clusters were present (TEM detection limit $\approx$1 nm). The formation of extremely small Pd clusters may be due to the stabilization effect of the polymer.

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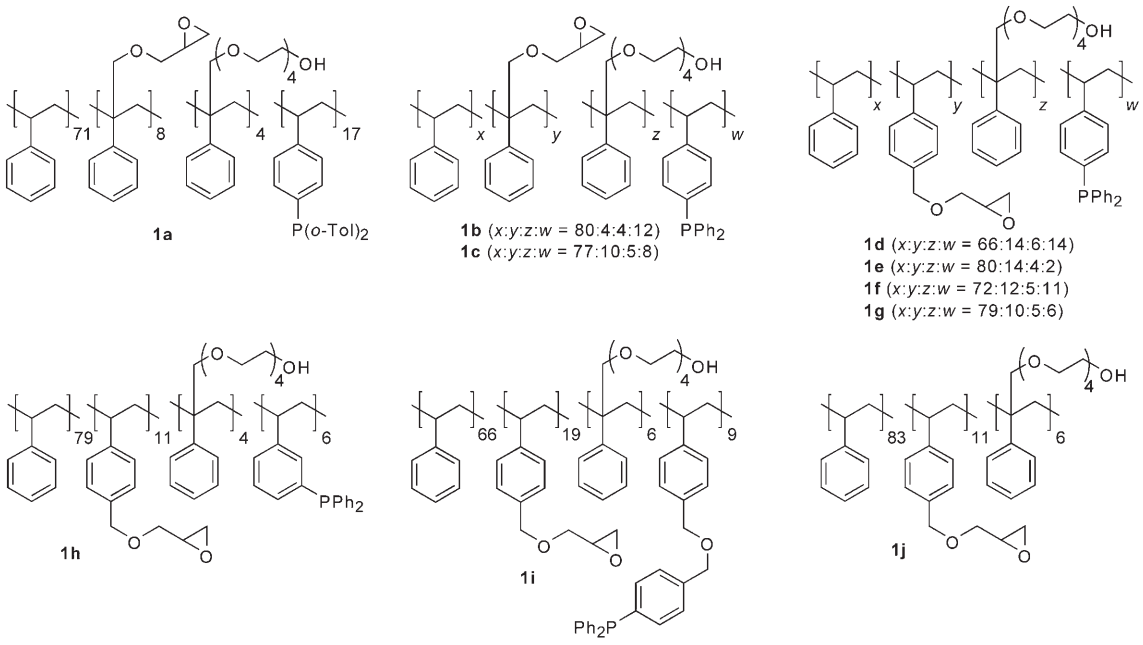
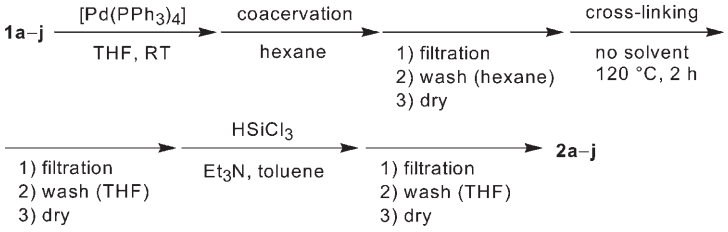


Scheme 2. Structures of the polymer supports of the PI Pd catalysts. Tol = tolyl.

Table 1. Preparation of phosphinated PI Pd catalysts.



Catalyst	Copolymer	P loading [mmol g^{-1}][a]	Pd loading [mmol g^{-1}][a]	P/Pd
2a	**1a**	1.1	0.25	4.3
2a′	**1a**	1.1	0.42	2.6
2b	**1b**	0.85	0.23	3.7
2c	**1c**	0.58	0.32	1.8
2d	**1d**	0.92	0.46	2.0
2e	**1e**	0.16	0.27	0.58
2f	**1f**	0.76	0.36	2.1
2g	**1g**	0.74	0.12	6.2
2h	**1h**	0.46	0.38	1.2
2i	**1i**	0.57	0.27	2.1
2j[b]	**1j**	0	0.67	0

[a] For determination of loadings, see reference [5d]. [b] Not treated with $HSiCl_3$.

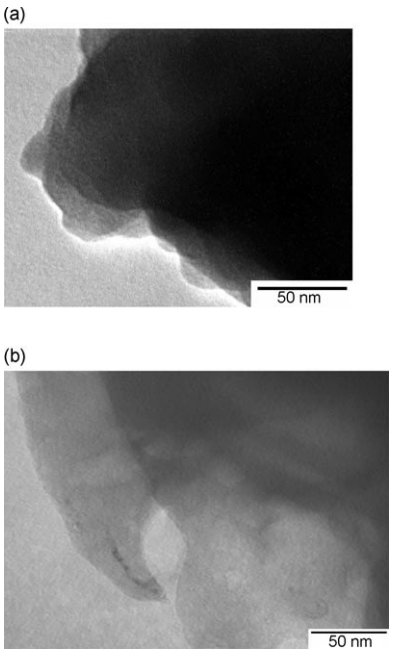


Figure 1. TEM images of a) **2a** and b) **2f**.

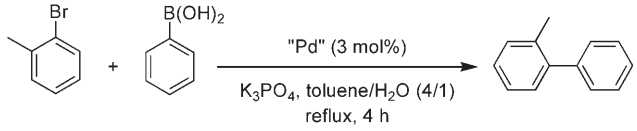
Application of Phosphinated PI Pd Catalysts to Suzuki–Miyaura Coupling

Palladium-catalyzed Suzuki–Miyaura coupling of organoboron compounds with aryl or vinyl halides is known as one of the most useful C–C bond-forming reactions.[13] Since the first report in 1981 with [Pd(PPh$_3$)$_4$] as catalyst,[14] the reaction has been widely used not only in academic laboratories but also in industry. Recently, heterogeneous catalysts for Suzuki–Miyaura coupling have attracted much attention.[15,16]

Phosphinated and non-phosphinated PI Pd catalysts **2c**, **e**–**i** and **2j**, respectively, were initially examined in the coupling reaction of 2-bromotoluene with phenylboronic acid without addition of any phosphine ligand (Table 2).

The structure of the polymer supports was found to influence the catalytic activity. PI Pd catalysts **2e**–**g**, which were prepared from the same type of the polymer support **1e**–**g**, were more effective than the catalysts derived from polymer **1c**, **1h**, or **1i**. The optimum ratio of diphenylphosphanyl

Table 2. Catalytic activities of phosphinated PI Pd catalysts ("Pd").



Entry	Catalyst (P/Pd)[a]	Yield[b] [%]	Leaching of Pd[c]
1	**2e** (0.58)	81	n.d.
2	**2f** (2.1)	96	n.d.
3	**2g** (6.2)	93	n.d.
4	**2c** (1.8)	64	n.d.
5	**2h** (1.2)	73	n.d.
6	**2i** (2.1)	70	n.d.
7	**2e** (0.58)	9	n.d.
8[d]	**2e** (0.58)	19	n.d.

[a] Ratio of diphenylphosphanyl groups in the polymer to Pd atoms. [b] Yield of isolated product. [c] Determined by XRF analysis; n.d. = not detected (<0.94%). [d] With the addition of 3 mol% of PPh_3 as ligand.

groups in the polymer to Pd atoms was found to be about 2:1, which afforded 2-methylbiphenyl in 96% yield. In contrast to the phosphinated PI Pd catalysts, the non-phosphinated **2j** did not show high catalytic activity even when triphenylphosphine was added as an external ligand. Leaching of the palladium was measured by fluorescence X-ray (XRF) analysis after removal of the catalyst, and no leaching was detected in all cases. This result indicates that small palladium clusters are strongly coordinated by both the π electrons of the benzene rings and the phosphines on the polymer support, but that this coordination does not come at the cost of decreased catalytic activity. The phosphines in the polymer support seem to play the important roles in this reaction of suppressing the leaching of palladium as well as increasing the catalytic activity by acting as ligands.

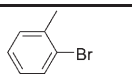
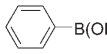
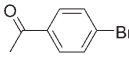
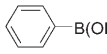
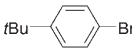
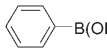
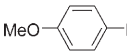
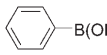
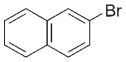
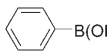
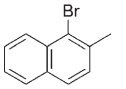
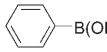
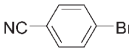
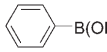
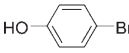
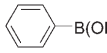
The results of the Suzuki–Miyaura couplings of a range of aryl halides with arylboronic acids mediated by the PI Pd catalysts are summarized in Table 3. The reaction proceeded smoothly with both electron-rich and electron-deficient aryl halides to afford the corresponding biaryl coupling products in high yields without any leaching of palladium.

Furthermore, PI Pd catalyst **2f** was recovered by simple filtration and reused several times for Suzuki–Miyaura coupling (Table 4) with no significant loss of activity, even up to the sixth cycle. It was confirmed by XRF analysis that no leaching of Pd from the catalyst occurred in all cases.[17] After the recovery and reuse of **2f** for five times, some aggregation of palladium clusters was observed by TEM analysis (Figure 2).[18]

Application of Phosphinated PI Pd Catalysts to Amination of Aryl Halides

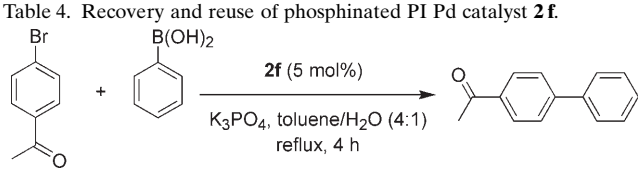
The palladium-catalyzed amination of aryl halides[19] has recently attracted much attention as a direct and efficient C–N bond-forming reaction for the synthesis of a variety of aryl amines, which are commonly found in biologically important compounds. Although many homogeneous palladium-catalyzed aminations have been reported,[20,21] there are

Table 3. Phosphinated PI Pd-catalyzed Suzuki–Miyaura coupling of various substrates without external phosphine ligands.[a]

Entry	Aryl halide	Boronic acid	Yield[b] [%]	Leaching of Pd[c]
1			96	n.d.
2			quant.	n.d.
3			quant.	n.d.
4			84	n.d.
5			94	n.d.
6			85	n.d.
7			85	n.d.
8			92	n.d.

[a] Reaction conditions: aryl halide (1.0 equiv), boronic acid (1.5 equiv), K_3PO_4 (1.5 equiv), **2f** (3 mol%, 0.36 mmol g^{-1}, P/Pd = 2.1), toluene/H_2O (4:1), reflux, 4 h. Workup conditions: reaction mixture was diluted with hexane, and the catalyst was filtered off and then extracted with EtOAc and brine. [b] Yield of isolated product. [c] Determined by XRF analysis.

Table 4. Recovery and reuse of phosphinated PI Pd catalyst **2f**.



Run	1	2	3	4	5
Yield[a] [%]	quant.	quant.	98	99	quant.
Leaching of Pd[b]	n.d.	n.d.	n.d.	n.d.	n.d.

[a] Yield of isolated product. [b] Determined by XRF analysis.

only a few reports of successful heterogeneous-catalyst systems for the same transformation.[22] In general, because harsh conditions of strong bases or polar solvents at high temperatures are necessary for palladium-catalyzed amination, there is a great possibility of poisoning, leaching, or aggregation of palladium. Therefore, the development of highly effective heterogeneous catalysts without any leaching of palladium has been a central issue for the amination of aryl halides.

With this in mind, we turned our attention to the use of our PI Pd catalyst systems in this reaction. Accordingly, we applied the phosphinated PI Pd catalysts **2a–i**, non-phosphinated PI Pd catalyst **2j**, and homogeneous catalyst $Pd(OAc)_2$ in the amination of iodobenzene with morpholine (Table 5). The initial results were not encouraging. To our disappointment, non-phosphinated PI Pd catalyst **2j** was not effective for amination in the absence of external phosphine ligands (Table 5, entry 1). On addition of P(*o*-Tol)$_3$ or **3**[23] as an external ligand to **2j**, the catalytic activity increased; however, some leaching of Pd was dectected by XRF analy-

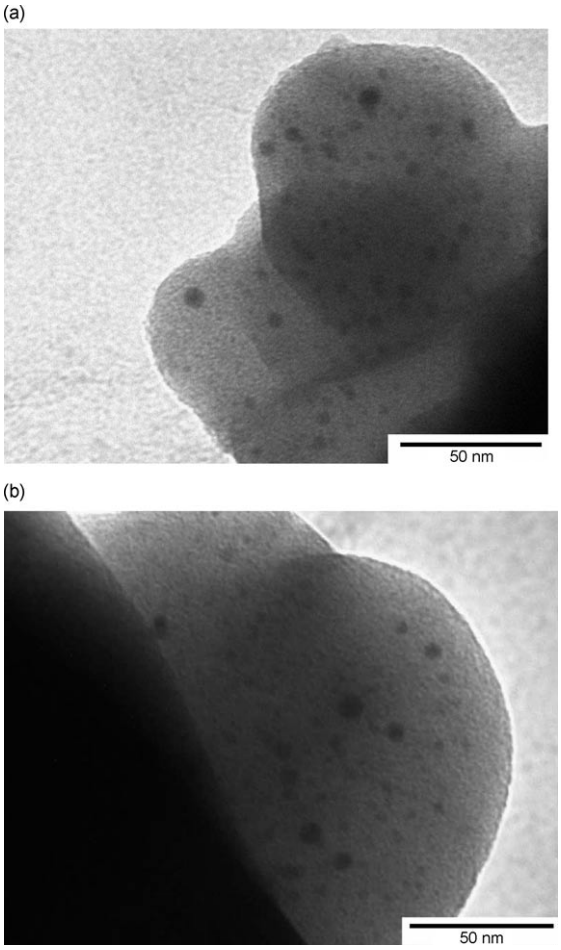
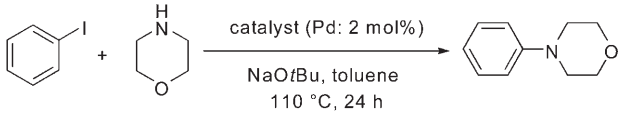
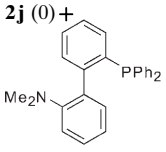


Figure 2. TEM images of **2f** after the fifth Suzuki–Miyaura coupling (magnification 600 000×) at two locations.

Table 5. Difference in catalytic activities in the amination reaction between phosphinated PI Pd catalysts and other types of catalysts.[a]



Entry	Catalyst (P/Pd)	Yield[b] [%]	Leaching of Pd[c] [%]
1	**2j** (0)	15	31
2[d]	**2j** (0)+P(*o*-Tol)$_3$	74	14
3[d]	**2j** (0)+ 	89	13
4	**2b** (3.7)	58	9
5	**2c** (1.8)	53	14
6	**2d** (2.0)	63	23
7	**2a** (4.3)	90	n.d.
8	**2a′** (2.6)	75	n.d.
9	Pd(OAc)$_2$+P(*o*-Tol)$_3$	86	–

[a] Reaction conditions: iodobenzene (1 equiv), morpholine (2.0 equiv), Pd catalyst (2.0 mol %), NaO*t*Bu (2.3 equiv), toluene (3.3 mL mmol^{-1} iodobenzene). [b] Yield of isolated product. [c] Determined by XRF analysis. [d] 4.0 mol % of phosphine was used.

sis (Table 5, entries 2 and 3). Gratifyingly though, phosphinated PI Pd catalysts **2b–d** showed higher catalytic activity than non-phosphinated **2j** even in the absence of external phosphine ligands; however, the problem of palladium leaching remained (Table 5, entries 4–6). Upon changing the substituent on the phosphorus atom from phenyl to *o*-tolyl, **2a** and **2a′** showed higher catalytic activities and suppressed the leaching of palladium (Table 5, entries 7 and 8). It is assumed that the reductive-elimination step of reactions mediated by these two catalysts proceeds more quickly[24] than with **2b–d** because they have bulkier phosphine moieties[25] on the polymer supports. As a result of this faster reductive elimination, polar Pd^{II} species such as Ar–Pd^{II}–X would be relatively short-lived and would therefore be less likely to leach out of the polymer supports into polar solvents, especially in the presence of a strong base such as NaO*t*Bu. Although **2a** and **2a′** were prepared from the same copolymer, **2a** with a higher phosphine/palladium ratio (P/Pd = 4.3) showed higher catalytic activity than **2a′** (P/Pd = 2.6). Heterogeneous PI Pd catalyst **2a** was found to show almost the same catalytic activity as the homogeneous system Pd(OAc)$_2$ with P(*o*-Tol)$_3$, which has a similar cone angle[26] to the phosphine moiety of **2a** (Table 5, entries 7 and 9).

To compare the catalytic activity of phosphinated PI Pd catalyst **2a** with those of non-phosphinated **2j** and the homogeneous Pd(OAc)$_2$ systems more accurately, we monitored the course of the conversion of iodobenzene and the yield of the desired aminated product by GC analysis (Figure 3). The reaction catalyzed by phosphinated **2a** without an external phosphine ligand (condition I) proceeded with essentially the same rate and in similar yields as the ho-

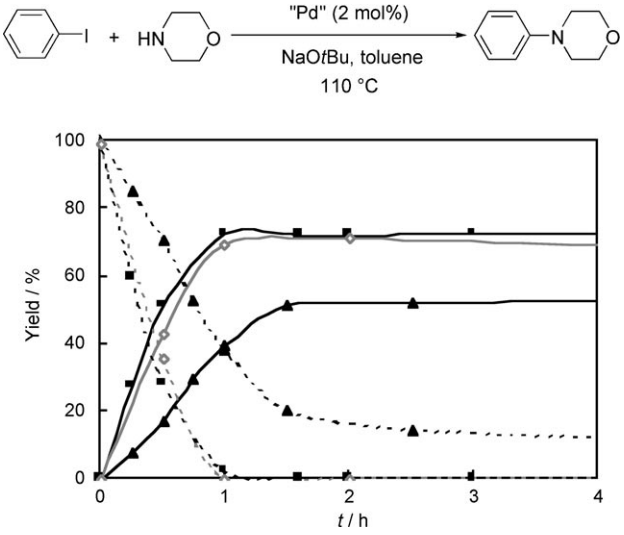
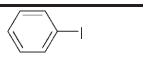
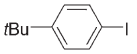
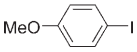
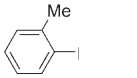
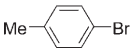
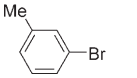
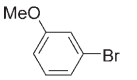
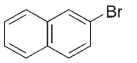
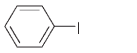
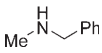
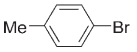
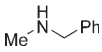
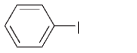
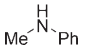
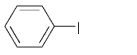
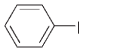
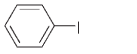
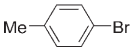
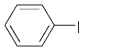
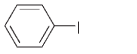
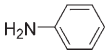


Figure 3. Reaction profiles of the amination of iodobenzene with morpholine in the presence of phosphinated PI Pd and other catalysts, showing the yield of *N*-phenylmorpholine determined by GC (solid lines) and the conversion of iodobenzene (dotted lines). Reaction conditions: aryl halide (1.0 equiv), morpholine (2.0 equiv), NaO*t*Bu (2.3 equiv), toluene (3.3 mL mmol^{-1} halide), 110 °C. Condition I (■): **2a** (2 mol %). Condition II (▲): **2j** (2 mol %) and P(*o*-Tol)$_3$ (4 mol %). Condition III (◇): Pd(OAc)$_2$ (2 mol %) and P(*o*-Tol)$_3$ (4 mol %).

mogeneous system (condition III). On the other hand, the same trasnsformation mediated by the non-phosphinated **2j** in the presence of P(*o*-Tol)$_3$ (condition II) showed a lower reaction rate despite the phosphine having almost the same pK_a[27] and cone angle. It is assumed that there are sufficiently reactive coordination sites in the phosphinated PI Pd catalyst. Almost the same catalytic activity as the homogeneous system was achieved without decrease in catalytic activity even on the polymer supports, because the polymer support is swollen in a polar solvent, which mimics to some extent the reaction conditions of the homogeneous systems. The coordination of both benzene rings[28] and phosphine moieties to palladium atoms would stabilize the palladium clusters and suppress leaching of palladium effectively.

Several examples of aminations of aryl halides with phosphinated PI Pd catalyst **2a** are summarized in Table 6. In all cases, no leaching of palladium was observed. Several types of secondary amines provided relatively good yields, whereas aniline did not give the desired product at all (Table 6, entry 17). Both aryl iodides and bromides with electron-donating groups afforded the desired aminated products in good yields.[29]

Table 6. Phosphinated PI Pd-catalyzed amination of various substrates without external phosphine ligands.[a]

Entry	Aryl halide	Amine	*t* [h]	Yield[b] [%]	Leaching of Pd[c]
1			2.5	90	n.d.
2			12	83	n.d.
3			24	71	n.d.
4			12	54	n.d.
5			12	83	n.d.
6			18	78	n.d.
7			18	69	n.d.
8			24	66	n.d.
9			5	55	n.d.
10			11	62	n.d.
11			2.5	51	n.d.
12			24	73	n.d.
13			24	44	n.d.
14		$HNnBu_2$	2.5	64	n.d.
15		$HNnBu_2$	11	67	n.d.
16		$HNCy_2$	12	22	n.d.
17			24	0	n.d.

[a] Reaction conditions: iodobenzene (1.0 equiv), **2a** (Pd: 2.0 equiv), NaO*t*Bu, toluene (3.3 mL mmol^{-1} iodobenzene). [b] Yield of isolated product. [c] Determined by XRF analysis. Cy = cyclohexyl.

To gain insight into the reaction mechanism, we investigated the profiles of the reactions with **2a** and homogeneous Pd(OAc)$_2$/P(*o*-Tol)$_3$ catalyst. Experiments showed that the efficiency of the reaction was dependent on the amount of base added (Figure 4). Phosphinated PI Pd catalyst **2a** showed different reaction rates and yields when the quantity of NaO*t*Bu was changed (Figure 4a). Higher catalytic activities of **2a** were observed when 2.3 or 3.5 equivalents of morpholine with respect to iodobenzene were used, but lower activity was shown in the case of 1.5 equivalents of morpholine, despite an excess amount of NaO*t*Bu with respect to aryl halide (>1 equiv). On the other hand, in the homogeneous system (Figure 4b), no difference in catalytic activity was observed under these reaction conditions. Amatore et al. reported the acceleration of the oxidative addition of aryl halides by anionic Pd^0 or Pd^{II} complexes, which were

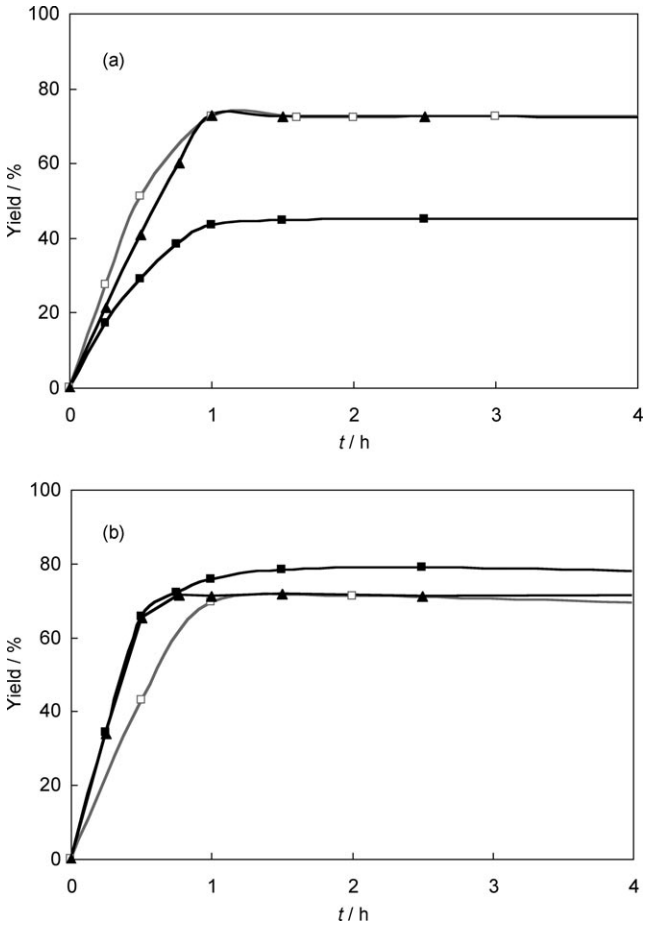


Figure 4. Reaction profiles of the amination catalyzed by a) **2a** and b) Pd(OAc)$_2$ with different amounts of NaO*t*Bu (■ = 1.5, □ = 2.3, ▲ = 3.5 equiv). Reaction conditions: iodobenzene (1.0 equiv), morpholine (2.0 equiv), toluene (3.3 mL mmol^{-1} halide), 110 °C, **2a** (2 mol %) (a) or Pd(OAc)$_2$ (2 mol %) and P(*o*-Tol)$_3$ (4 mol %) (b).

generated by the coordination of alkoxide bases such as NaO*t*Bu to palladium atoms.[30,31] In the case of **2a**, Pd^0 clusters would be immobilized between the hydrophobic benzene moieties in the polymer support rather than the hydrophilic tetraethyleneglycol or hydroxy moieties of the polymer support, because nonpolar Pd^0 clusters have a greater interaction with hydrophobic sites. Thus, to generate an anionic Pd complex with Pd^0 clusters, a large excess of ionic NaO*t*Bu may be necessary for incorporation into the hydrophobic benzene sites of the polymer support (Figure 4a). On the other hand, in the case of the homogeneous catalyst, the Pd^0 species and NaO*t*Bu would readily generate anionic complexes because there is a sufficient amount of NaO*t*Bu with respect to the catalytic amount of palladium in situ. Therefore, it is supposed that catalytic activity would not be affected by the amount of NaO*t*Bu (Figure 4b).

Next, it was revealed that the amount of morpholine does not affect the reaction rate and yield of **2a**-catalyzed amination, as judged from GC analysis (Figure 5a). On the other hand, a large difference in catalytic activity was observed in the case of the homogeneous system (Figure 5b). Hartwig and co-workers reported the effect of coordination of amines to palladium complexes on the rate of oxidative addition.[21d] They demonstrated that oxidative addition of aryl halides to Pd(binap)(amine) complexes (binap = 2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl), generated by the coordination of amines to Pd(binap) in situ, is slower than that to the corresponding Pd(binap) complex. Therefore, in the case of the homogeneous catalyst system shown in Figure 5b, the catalytic activity may be decreased due to the coordination of the amine, which poisons the palladium sterically and/or electrically. On the other hand, in the case of the phosphinated PI Pd catalyst, palladium clusters would be stabilized by weak interactions of the benzene rings[11,32] in the polymer support. Therefore, poisoning of palladium clusters by amines would be suppressed even in the presence of an excess of the amine. A similar effect of the polymer supports of phosphinated PI Pd catalysts on the suppression of poisoning was also observed previously in the hydrogenation[5i] of alkynes. Even in the presence of phosphines, selective semi-hydrogenation of alkynes proceeded by using phosphinated PI Pd catalysts. Thus, it is supposed that the decrease in catalytic activity due to poisoning by amines is suppressed by the stabilization effect of the polymer support.

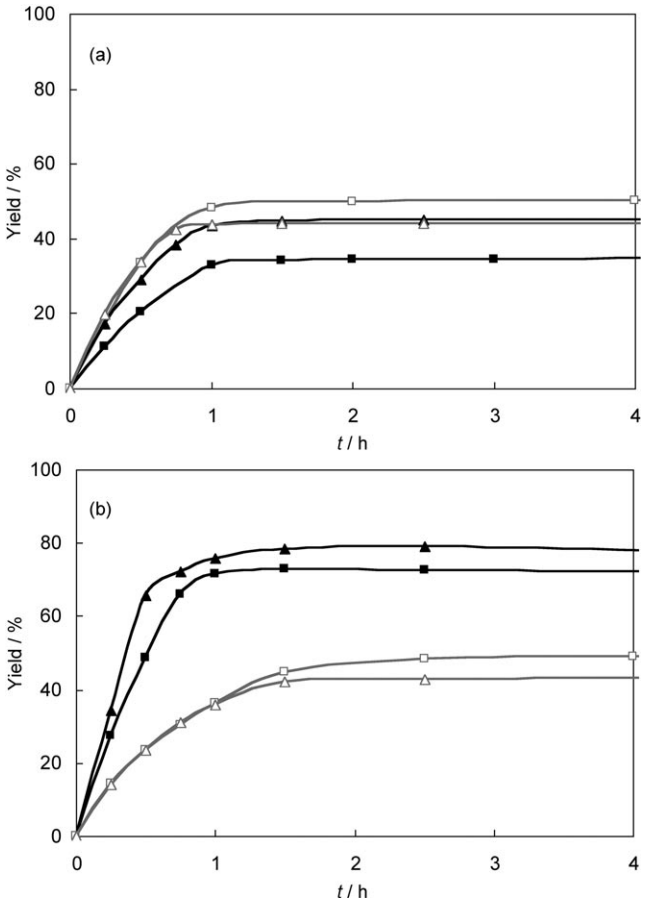
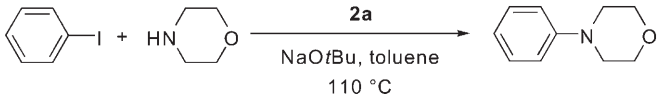


Figure 5. Reaction profiles of the amination catalyzed by a) **2a** and b) $Pd(OAc)_2$ with different amounts of morpholine (■ = 1.0, □ = 1.3, ▲ = 2.0, △ = 3.0 equiv). Reaction conditions: iodobenzene (1.0 equiv), NaO*t*Bu (1.5 equiv), toluene (3.3 mL mmol^{-1} halide), 110 °C, **2a** (2 mol %) (a) or $Pd(OAc)_2$ (2 mol %) and P(*o*-Tol)$_3$ (4 mol %) (b).

Importantly, the heterogeneous catalysts can be recovered simply and reused several times. In phosphinated PI Pd-catalyzed amination, a significant decrease in catalytic activity was observed when the catalyst was recovered by simple filtration and reused as it was (method A in Table 7). It is believed that the decreased catalytic activity is due to the oxidation of phosphine moieties of the polymer support and aggregation of the palladium clusters. Indeed, after the first reaction in method A, oxidation of phosphine moieties was observed by ^{31}P SR-MAS NMR analysis,[33] and formation of large palladium clusters (3–10 nm) were found by TEM analysis (Figure 6a and b), whereas no such larger clusters were detected before the reaction. On the other hand, when the recovered catalyst was treated with $HSiCl_3$ after each recovery of the catalyst to reduce the oxidized phosphine moieties in the polymer support (method B), the yields of the

Table 7. Recovery and reuse of phosphinated PI Pd catalysts in amination.[a]



Run	Method A		Method B	
	Yield[b] [%]	Leaching of Pd[c] [%]	Yield[b] [%]	Leaching of Pd[c] [%]
1	88	n.d.	92	n.d.
2	53	n.d.	90	n.d.
3	16	n.d.	81	n.d.

[a] Reaction conditions: iodobenzene (1.0 equiv), morpholine (2.0 equiv), NaO*t*Bu (2.3 equiv), toluene (3.3 mL mmol^{-1} iodobenzene), 12–20 h. Method A: 2 mol % Pd, not treated with $HSiCl_3$ after recovery of catalyst. Method B: 5 mol % Pd, reduced with $HSiCl_3$ after recovery of catalyst. [b] Yield determined by GC. [c] Determined by XRF analysis.

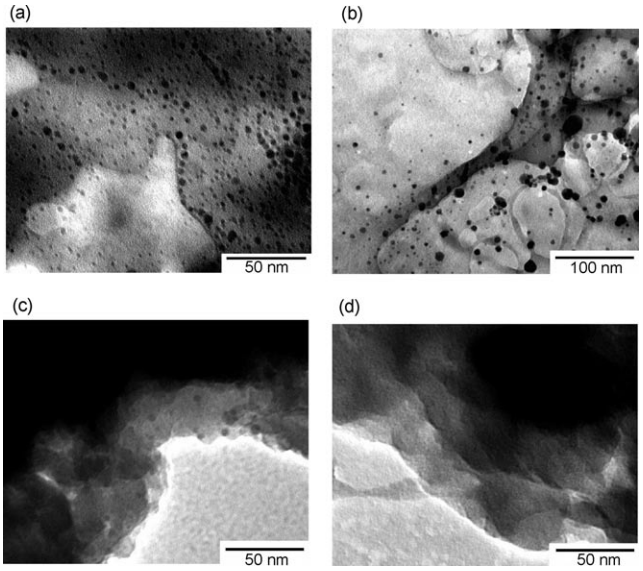


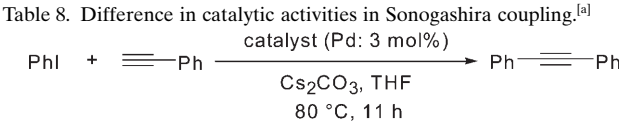
Figure 6. TEM images of **2a** a) after first amination with method A, b) after third amination with method A, c) after first amination and reduction with $HSiCl_3$ with method B, and d) after third amination and reduction with $HSiCl_3$ with method B (magnification 300000–600000×).

subsequent reactions with the catalyst sample were improved. After recovery of the catalyst in method B, aggregation of the palladium clusters was suppressed to 1–3 nm in size (Figure 6c and d); this observation suggests that non-oxidized phosphine moieties would stabilize palladium clusters.

Application of Phosphinated PI Pd Catalysts to Sonogashira Coupling

Phosphinated PI Pd catalysts can be also used in the Sonogashira coupling[34] between aryl halides and terminal alkynes (Table 8). Several types of phosphinated PI Pd catalysts showed higher catalytic activities than non-phosphinated catalyst **2j** without the addition of phosphine ligands. However, some leaching of palladium was observed even in phosphinated PI Pd catalysts by XRF analysis. It is assumed that polar palladium(II) species have a weak coordination affinity to the polymer support because the *trans*-metalation of palladium(II) species with cesium acetylide is slow. As for the amount of phosphine moieties on the polymer support, **2g**, which has a larger amount of phosphine, showed a higher catalytic activity than the other catalysts prepared from similar polymers with small P/Pd ratios and also suppressed the leaching of palladium (Table 8, entries 2–4).

Table 8. Difference in catalytic activities in Sonogashira coupling.[a]

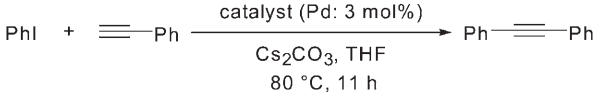


Entry	Catalyst (P/Pd)	Yield [%][b]	Leaching of Pd [%][c]
1	**2a** (4.3)	55	4
2	**2e** (0.58)	28	16
3	**2d** (2.0)	56	8
4	**2g** (6.2)	80	3
5	**2c** (1.8)	84	3
6	**2i** (2.1)	56	12
7	**2h** (1.2)	50	15
8[d]	**2j** (0)	22	54

[a] Reaction conditions: iodobenzene (1.0 equiv), phenylacetylene (1.5 equiv), PI Pd catalyst (Pd: 3 mol%), Cs_2CO_3 (1.5 equiv), THF, 110°C, 11 h. [b] Yield determined by GC. [c] Determined by XRF analysis. [d] With non-phosphinated PI Pd catalyst without externally added phosphine ligands.

To suppress the leaching of palladium from the polymer support, we added copper(I) iodide to accelerate the *trans*-metalation step (Table 9). For both PI Pd catalysts **2c** and **2d**, the catalytic activities increased, and leaching of palladium was suppressed by adding two equivalents of copper(I) iodide with respect to the palladium atoms. In general, *trans*-metalation is accelerated by addition of copper(I) salts because the Ar–Pd^{II}–X species shows better affinity to copper acetylides than alkaline-metal acetylides alone. Therefore, both catalytic activity and suppression of palladium leaching was improved because the polar Ar–Pd^{II}–X species was smoothly converted into the less-polar Ar–Pd^{II}–acetylide.

Table 9. Effect of CuI in phosphinated PI Pd-catalyzed Sonogashira coupling.[a]



Entry	Catalyst	Additive	Yield [%][b]	Leaching of Pd [%][c]
1	**2c**	–	84	3
2	**2c**	CuI[d]	98	n.d.
3	**2d**	–	56	8
4	**2d**	CuI[d]	quant.	7

[a] Reaction conditions: iodobenzene (1.0 equiv), phenylacetylene (1.5 equiv), Cs_2CO_3 (1.5 equiv), THF, 110°C, 11 h. [b] Yield determined by GC. [c] Determined by XRF analysis. [d] 6 mol%.

Phosphinated PI Pd catalyst **2c** was used in the Sonogashira coupling reaction of other types of substrates (Scheme 3). Aryl iodides with electron-withdrawing groups afforded coupling products in good yields without leaching of palladium. On the other hand, some leaching was observed in the reaction between 1-iodonaphthalene and phenylacetylene.

Conclusions

In summary, we have immobilized palladium clusters in phosphinated polymer supports to obtain phosphinated PI Pd catalysts. Their application to the amination of aryl halides for C–N bond-forming reactions, as well as to the Suzuki–Miyaura and Sonogashira coupling reactions for C–C bond formation, has been demonstrated. These catalysts

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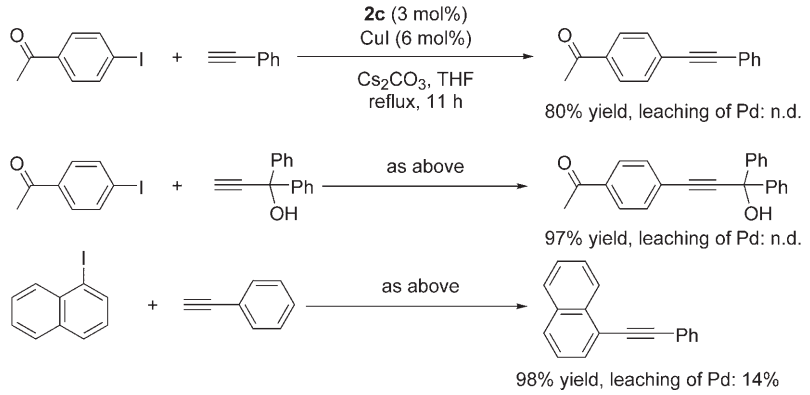

Scheme 3. Phosphinated PI Pd-catalyzed Sonogashira coupling with other types of substrate.

showed good activities without the addition of external phosphine ligands and gave almost the same level of catalytic activity as homogeneous catalysts in amination. No leaching of palladium was observed after the reaction by XRF analysis even under the harsh reaction conditions of strong base and high temperature. It was revealed that the phosphinated PI Pd catalysts did not suffer from poisoning of the metal by amines. Moreover, they were recovered by simple filtration and reused several times without loss of activity, and no leaching of palladium in both amination and Suzuki–Miyaura coupling was observed. These effects can be ascribed to electrical and steric stabilization of palladium clusters by both the phosphine moieties and the benzene rings on the inside of the polymer supports. The methodologies described herein offer simplified and useful protocols for highly active heterogeneous catalysts without the addition of phosphine ligands.

Experimental Section

General Methods

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a JEOL ECX-600 or ECX-400 spectrometer in $CDCl_3$ unless otherwise noted. Tetramethylsilane (TMS; $\delta = 0$ ppm) and $CDCl_3$ ($\delta = 77.0$ ppm) served as the internal standard for ^{1}H NMR and ^{13}C NMR spectroscopy, respectively. For ^{31}P NMR spectroscopy, 85% H_3PO_4 was the external standard. Preparative thin-layer chromatography (PTLC) was carried out with a Wakogel B-5F chromatograph. Toluene, tetrahydrofuran (THF), *n*-hexane, and methanol were purchased from Wako Pure Chemical Industries, Ltd. and used without further purification. Distilled water was employed for the aqueous reactions. All other solvents were purified based on standard procedures.

Syntheses

Di-*o*-tolyl-(4-vinylphenyl)phosphine: 4-Bromostyrene (3.35 g, 18.3 mmol) was dissolved in THF (67 mL) at room temperature, and *n*-butyllithium (1.6 M, 20.1 mmol) was added to this solution. The mixture was stirred for 10 min at −78 °C, and chlorodi-*o*-tolylphosphine (5.00 g, 20.1 mmol) was added dropwise to this solution. After the mixture was stirred for 2 h at −78 °C and for 14 h at room temperature, saturated aqueous NH_4Cl was added. The mixture was extracted with ethyl acetate and washed with saturated aqueous $NaHCO_3$ and brine. The organic layers were dried over anhydrous $MgSO_4$, filtered, and evaporated to give a crude product. This crude product was purified by silica-gel column chromatography (hexane/ethyl acetate = 30:1, 20:1, 10:1) to give di-*o*-tolyl-(4-vinylphenyl)phosphine (3.30 g, 57%). ^{1}H NMR ($CDCl_3$, 600 MHz): $\delta = 2.39$ (s, 6H), 5.27 (d, $J = 11.0$ Hz, 1H), 5.78 (d, $J = 18.5$ Hz, 1H), 6.75 (dd, $J = 6.9$, 3.4 Hz, 2H), 7.07 (t, $J = 7.6$ Hz, 2H), 7.20–7.26 (m, 6H), 7.37 ppm (dd, $J = 6.8$, 1.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 21.1, 21.2, 114.6, 126.1, 126.4, 126.4, 128.7, 130.0, 130.1, 132.8, 134.4, 134.6, 135.0, 135.1, 135.2, 136.4, 137.9, 142.3, 142.5 ppm; ^{31}P NMR ($CDCl_3$, 162 MHz): $\delta = -21.0$ ppm.

Diphenyl-(4-vinylphenyl)phosphine:[35] 4-Bromostyrene (5.60 g, 30.6 mmol) was dissolved in THF (110 mL) at room temperature, and *n*-butyllithium (1.6 M, 36.7 mmol) was added to this solution. The mixture was stirred for 30 min at −78 °C, and chlorodiphenylphosphine (8.09 g, 36.7 mmol) was added dropwise to this solution. After the mixture was stirred for 3 h at −78 °C and for 1 h at room temperature, saturated aqueous NH_4Cl was added. The mixture was extracted with ethyl acetate and washed with saturated aqueous $NaHCO_3$ and brine. The organic layers were dried over anhydrous $MgSO_4$, filtered, and evaporated to give a crude product. This crude product was purified by silica-gel column chromatography (hexane/ethyl acetate = 30:1, 20:1, 10:1) to give diphenyl-(4-vinylphenyl)-phosphine (7.59 g, 86%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 5.23$ (d, $J =$ 10.8 Hz, 1H), 5.73 (d, $J = 17.6$ Hz, 2H), 6.66 (dd, $J = 17.6$, 10.8 Hz, 1H), 7.27–7.31 ppm (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 114.4$, 126.3, 128.5, 128.7, 133.6, 133.8, 134.0, 136.4, 137.2, 137.9 ppm; ^{31}P NMR ($CDCl_3$, 162 MHz) $\delta = -5.30$ ppm.

1a (Scheme 2): Styrene (2.00 g, 19.2 mmol), 2-[(2-phenylallyloxy)methyl]oxirane (521 mg, 2.74 mmol), tetraethyleneglycol mono-2-phenyl-2-propenyl ether (853 mg, 2.74 mmol), di-*o*-tolyl-(4-vinylphenyl)phosphine (867 mg, 2.74 mmol), and 2,2′-azobis(isobutyronitrile) (45.0 mg, 0.274 mmol) were mixed in *N*,*N*-dimethylformamide (DMF; 3.3 mL). The mixture was stirred for 24 h at 75 °C and then cooled to room temperature. The resulting polymer solution was poured slowly into cooled methanol. The precipitated polymer was collected by filtration, washed with methanol several times, and dried for 24 h under reduced pressure to afford **1a** (2.54 g, 60%). The molar ratio of the monomer was determined by ^{1}H NMR spectroscopic analysis (styrene/2-[(2-phenylallyloxy)methyl]oxirane/tetraethyleneglycol mono-2-phenyl-2-propenyl ether/di-*o*-tolyl-(4-vinylphenyl)phosphine = 71:8:4:17). ^{31}P NMR ($CDCl_3$, 162 MHz): $\delta =$ −21.6 ppm.

1f (Scheme 2): Styrene (3.00 g, 28.8 mmol), 4-vinylbenzyl glycidyl ether (782 mg, 4.11 mmol), tetraethyleneglycol mono-2-phenyl-2-propenyl ether (1.28 g, 4.11 mmol), diphenyl-(4-vinylphenyl)phosphine (1.18 g, 4.11 mmol), and 2,2′-azobis(isobutyronitrile) (67.5 mg, 0.411 mmol) were mixed in DMF (4.8 mL). The mixture was stirred for 24 h at 70 °C and then cooled to room temperature. The resulting polymer solution was poured slowly into cooled methanol. The precipitated polymer was collected by filtration, washed with methanol several times, and dried for 24 h under reduced pressure to afford **1f** (3.57 g, 57%). The molar ratio of the monomer was determined by ^{1}H NMR spectroscopic analysis (styrene/4-vinylbenzyl glycidyl ether/tetraethyleneglycol mono-2-phenyl-2-propenyl ether/diphenyl-(4-vinylphenyl)phosphine = 72:12:5:11). $M_w =$ 49330, $M_n = 25692$, $M_w/M_n = 1.92$ (gel-permeation chromatography; GPC).

2a (Table 1): Copolymer **1a** (1.17 g) was dissolved in THF (27 mL) at room temperature, and $[Pd(PPh_3)_4]$ (293 mg) was added to this solution as a core ($[Pd(PPh_3)_4]$ was dissolved). The mixture was stirred for 48 h at this temperature under air. Hexane (40 mL) was then slowly added to the mixture at room temperature. Coacervates were found to envelop the core dispersed in the medium. The mixture was left to stand at room temperature for 12 h, and the catalyst capsules were then washed with

hexane several times and dried at room temperature under reduced pressure for 6 h. Next, the catalyst capsules were stirred at 120 °C for 3 h under air to cross-link the microencapsulated palladium. After cooling, the cross-linked solid was washed with THF several times and dried under reduced pressure for 12 h. The resulting black solid (1.06 g), trichlorosilane (786 mg, 5.8 mmol), and triethylamine (708 mg, 7.00 mmol) were stirred in toluene (27 mL) for 24 h at 100 °C under argon to reduce the phosphine oxide moieties. The mixture was cooled to room temperature, the reaction was quenched by careful addition of methanol (15 mL), and the catalyst was washed with hexane and THF several times and dried at room temperature under reduced pressure for 12 h to give **2a** (1.11 g). Loading of palladium metal = 0.25 mmol g^{-1}, P/Pd = 4.3:1.0. The loading of di-*o*-tolylphosphanyl groups in the polymer support was determined by the ratio of monomers introduced into the copolymer. ^{31}P SR-MAS NMR ($CDCl_3$, 162 MHz): $\delta = 0.00$ ppm.

2f (Table 1): Copolymer **1f** (1.00 g) was dissolved in THF (25 mL) at room temperature, and $[Pd(PPh_3)_4]$ (0.50 g) was added to this solution as a core ($[Pd(PPh_3)_4]$ was dissolved). The mixture was stirred for 24 h at this temperature under air. Hexane (30 mL) was then slowly added to the mixture at room temperature. Coacervates were found to envelop the core dispersed in the medium. The mixture was left to stand at room temperature for 12 h, and the catalyst capsules were then washed with hexane several times and dried at room temperature for 24 h. Next, the catalyst capsules were stirred at 120 °C for 2 h under air to cross-link the microencapsulated palladium. After cooling, the cross-linked solid was washed with THF several times and dried under reduced pressure for 12 h. The resulting black solid (1.09 mg), trichlorosilane (754 mg, 5.57 mmol), and triethylamine (620 mg, 6.13 mmol) were stirred in toluene (22 mL) for 12 h at 100 °C to reduce the phosphine oxide moieties. The mixture was cooled to room temperature, the reaction was quenched by careful addition of methanol (20 mL), and the catalyst was washed with hexane and THF several times and dried at room temperature for 12 h to give **2f** (0.98 g). Loading of palladium metal = 0.36 mmol g^{-1}, P/Pd = 2.10:1.00. The loading of diphenylphosphanyl groups in the polymer support was determined by the ratio of monomers introduced into the copolymer. ^{31}P SR-MAS NMR ($CDCl_3$, 162 MHz): $\delta = -5.0$ ppm.

Determination of Palladium Loading

PI Pd catalyst **2a** (22.5 mg) was placed in a 50-mL test tube, and sulfuric acid (95%, 1.0 mL) was added. The mixture was heated at 180 °C for 30 min. After the mixture was cooled to room temperature, fuming nitric acid (0.5 mL) was added, and the mixture was heated further at 180 °C to decompose the polymer. The mixture was again cooled to room temperature, water (5 mL) was added, and the mixture was heated at 180 °C again for complete dissolution. The solution was adjusted to 10 mL with water, and the amount of palladium metal was measured by XRF analysis to determine the loading of palladium.

Typical Experimental Procedure for Suzuki–Miyaura Coupling

2-Methylbiphenyl[36] (Table 3, entry 1): 2-Bromotoluene (68.4 mg, 0.400 mmol), phenylboronic acid (73.2 mg, 0.600 mmol), **2b** (0.0120 mmol, 3 mol%), and K_3PO_4 (0.600 mmol) were combined in toluene/H_2O (4:1, 4 mL) under argon. The mixture was stirred f or 4 h under reflux conditions. After the mixture was cooled to room temperature, hexane was added to quench the reaction, and the catalyst was collected by filtration, washed with ethyl acetate and water, and then dried and reused. The filtrate was extracted with ethyl acetate and washed with brine. The organic layers were dried over anhydrous Na_2CO_3, filtered, and evaporated to give a crude product. The volume of the residue was adjusted to 5 mL with THF to give a sample for XRF analysis for the measurement of palladium leaching. The sample solution after measurement of leaching was evaporated, and the residual crude product was purified by PTLC on silica gel (hexane) to afford 2-methylbiphenyl (64.8 mg, 96%). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 2.26$ (s, 3H), 7.21–7.42 ppm (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 20.4$, 125.7, 126.7, 127.2, 128.0, 129.2, 129.8, 130.3, 135.3, 141.9 ppm.

4-Acetylbiphenyl[37] (Table 3, entry 2): ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta =$ 2.60 (s, 3H), 7.35–7.46 (m, 3H), 7.58–7.66 (m, 4H), 8.00 ppm (d, $J =$ 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 26.5$, 127.1, 127.1, 128.1, 128.8, 128.8, 135.7, 139.7, 145.6, 197.6 ppm.

4-*tert*-Butylbiphenyl[37] (Table 3, entry 3): ^{1}H NMR ($CDCl_3$, 600 MHz): $\delta = 1.35$ (s, 9H), 7.31 (t, $J = 8.4$ Hz, 1H), 7.41 (t, $J = 8.4$ Hz, 2H), 7.45 (d, $J = 9.0$ Hz, 2H), 7.53 (d, $J = 9.0$ Hz, 2H), 7.58 ppm (dd, $J = 8.4$, 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 31.4$, 34.5, 125.7, 126.8, 127.0, 127.0, 128.7, 138.3, 141.0, 150.2 ppm.

4-Methoxybiphenyl[36] (Table 3, entry 4): ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 3.85$ (s, 3H), 6.98 (d, $J = 8.4$ Hz, 2H), 7.30 (t, $J = 6.8$ Hz, 1H), 7.41 (t, $J = 8.0$ Hz, 2H), 7.54 ppm (t, $J = 8.0$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 55.3$, 114.2, 126.6, 126.7, 128.1, 128.7, 133.7, 140.8, 159.1 ppm.

2-*o*-Tolylnaphthalene[38] (Table 3, entry 5): ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 2.30$ (s, 3H), 7.25–7.30 (m, 4H), 7.44–7.49 (m, 3H), 7.76 (s, 1H), 7.79–7.86 ppm (m, 3H).

2-Methyl-1-phenylnaphthalene[39] (Table 3, entry 6): ^{1}H NMR ($CDCl_3$): $\delta = 2.21$ (s, 3H), 7.22–7.43 (m, 9H), 7.72–7.81 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 20.8$, 124.7, 125.8, 126.1, 126.9, 127.2, 127.7, 128.3, 128.6, 130.1, 131.9, 132.9, 133.0, 138.1, 139.8 ppm.

4-Cyano-2′-methylbiphenyl[36] (Table 3, entry 7): ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 2.25$ (s, 3H), 7.19 (d, $J = 7.1$ Hz, 1H), 7.25–7.33 (m, 3H), 7.44 (d, $J = 8.0$ Hz, 2H), 7.71 ppm (d, $J = 7.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 20.3$, 110.7, 118.9, 126.1, 128.3, 129.4, 130.0, 130.6, 131.9, 135.0, 140.0, 146.8 ppm.

4-Hydroxy-2′-methylbiphenyl[40] (Table 3, entry 8): ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 2.27$ (s, 3H), 6.87 (t, $J = 7.5$ Hz, 2H), 7.18–7.25 ppm (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 20.5$, 114.9, 125.7, 127.0, 129.8, 130.3, 130.4, 134.5, 135.4, 141.4, 154.3 ppm.

Typical Experimental Procedure for Amination

N-Phenylmorpholine[41] (Table 6, entry 1): Iodobenzene (61.2 mg, 0.300 mmol), morpholine (52.3 mg, 0.600 mmol), **2a** (24.0 mg, 0.006 mmol, 2 mol%), and NaO*t*Bu (66.3 mg, 0.690 mmol) were combined in toluene (1.0 mL) under argon. The mixture was stirred for 2.5 h under reflux conditions. After the mixture was cooled to room temperature, hexane (3 mL) was added to quench the reaction, and the catalyst was collected by filtration, washed with hexane, and dried. The filtrate was evaporated to give a crude product. The volume of the residue was adjusted to 5 mL with THF to give a sample for XRF analysis for the measurement of palladium leaching. The sample solution after measurement of leaching was evaporated, and the residual crude product was purified by PTLC on silica gel (hexane/ethyl acetate = 6:1) to afford *N*-phenylmorpholine (44.1 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 3.16$ (t, $J = 4.8$ Hz, 4H), 3.85 (t, $J = 4.8$ Hz, 4H), 6.88 (t, $J = 7.4$ Hz, 1H), 6.92 (d, $J = 8.2$ Hz, 2H), 7.28 ppm (dd, $J = 7.4$, 8.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 49.2, 66.9, 115.7, 120.0, 129.1, 151.2 ppm.

4-(4-*tert*-Butylphenyl)morpholine[42] (Table 6, entry 2): ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 1.30$ (s, 9H), 3.15 (t, $J = 4.4$ Hz, 4H), 3.86 (t, $J =$ 4.4 Hz, 4H), 6.87 (d, $J = 8.9$ Hz, 2H), 7.29 ppm (d, $J = 8.9$ Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 31.4, 33.8, 49.5, 66.7, 115.3, 125.9, 142.6, 149.0 ppm.

N-(4-Methoxyphenyl)morpholine[41] (Table 6, entry 3): ^{1}H NMR (600 MHz, $CDCl_3$): $\delta =$ 3.05 (t, $J = 4.6$ Hz, 4H), 3.78 (s, 3H), 3.86 (t, $J =$ 4.6 Hz, 4H), 6.85–6.90 ppm (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 50.8, 55.5, 67.0, 114.6, 117.8, 145.5, 153.9 ppm.

N-(2-Methylphenyl)morpholine[43] (Table 6, entry 4): ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 2.32$ (s, 3H), 2.91 (t, $J = 4.5$ Hz, 4H), 3.85 (t, $J = 4.5$ Hz, 4H), 7.00 (d, $J = 7.4$ Hz, 1H), 7.03 (d, $J = 7.4$ Hz, 1H), 7.18 (d, $J = 7.4$ Hz, 1H), 7.19 ppm (d, $J = 7.4$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 17.7, 52.3, 67.5, 119.0, 123.5, 126.6, 131.2, 132.6, 151.4 ppm.

N-(4-Methylphenyl)morpholine[41] (Table 6, entry 5): ^{1}H NMR (600 MHz, $CDCl_3$): $\delta =$ 2.27 (s, 3H), 3.10 (t, $J = 4.4$ Hz, 4H), 3.85 (t, $J = 4.4$ Hz, 4H), 6.83 (d, $J = 8.4$ Hz, 2H), 7.08 ppm (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 20.4, 49.8, 67.0, 116.1, 129.6, 129.6, 149.2 ppm.

N-(3-Methyphenyl)morpholine[49] (Table 6, entry 6): ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 2.32$ (s, 3H), 3.12–3.15 (m, 4H), 3.83–3.86 (m, 4H), 6.69–6.72

(m, 3H), 7.14–7.20 ppm (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=22.0, 49.7, 67.1, 113.2, 116.8, 121.1, 129.3, 139.1, 151.5 ppm.

N-(3-Methoxyphenyl)morpholine[44] (Table 6, entry 7): ^{1}H NMR (600 MHz, $CDCl_3$): δ= 3.17 (t, J=4.6 Hz, 4H), 3.81 (s, 3H), 3.86 (t, J= 4.6 Hz, 4H), 6.59–6.45 (m, 3H), 7.21 ppm (t, J=8 L Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=49.2, 55.2, 66.9, 102.2, 104.7, 108.4, 129.8, 152.7, 160.0 ppm.

4-(2-Naphthyl)morpholine[45] (Table 6, entry 8): ^{1}H NMR (600 MHz, $CDCl_3$): δ= 3.25 (t, J=4.1 Hz, 4H), 3.91 (t, J=4.1 Hz, 4H), 7.11 (d, J= 2.0 Hz, 1H), 7.25 (dd, J=8.9, 2.8 Hz, 1H), 7.30 (dt, J=8.2, 1.4 Hz, 1H), 7.41 (dt, J=6.8, 1.4 Hz, 1H), 6.69–7.75 ppm (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=49.9, 67.0, 110.2, 119.0, 123.6, 126.4, 126.9, 127.4, 128.8, 128.9, 134.6, 149.2 ppm.

N-Benzyl-*N*-methylaniline[46] (Table 6, entry 9): ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.95 (s, 3H), 4.47 (s, 2H), 6.66–6.72 (m, 3H), 7.20–7.31 ppm (m, 7H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=38.4, 56.6, 112.2, 116.4, 126.7, 126.7, 128.5, 129.0, 138.9, 149.6 ppm.

N-Benzyl-*N*-methyl-*p*-methylaniline[47] (Table 6, entry 10): ^{1}H NMR (600 MHz, $CDCl_3$): δ= 2.24 (s, 3H), 2.96 (s, 3H), 4.49 (s, 2H), 6.63 (d, J=8.6 Hz, 2H), 7.00 (d, J=8.7 Hz, 2H) 7.28–7.31 ppm (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=20.2, 38.6, 57.0, 112.7, 125.5, 126.8, 128.3, 129.7, 139.2, 147.8 ppm.

N-Methyl-*N*-phenylaniline[41] (Table 6, entry 11): ^{1}H NMR (600 MHz, $CDCl_3$): δ=3.30 (s, 3H), 6.95 (dt, J=7.2, 1.2 Hz, 2H), 7.02 (dd, J=8.8, 1.2 Hz, 4H), 7.26 ppm (dd, J=8.8, 7.2 Hz, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=40.2, 120.2, 121.2, 129.1, 148.9 ppm.

N-Phenylpiperidine[48] (Table 6, entry 12): ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.55–1.59 (m, 2H), 1.69–1.73 (m, 4H), 3.15 (t, J=5.5 Hz, 4H), 6.82 (t, J=6.9 Hz, 1H), 6.94–6.98 (d, J=8.3 Hz, 2H), 7.23–7.26 ppm (t, J= 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=26.3, 29.3, 51.2, 117.1, 119.6, 129.5, 152.8 ppm.

N-Phenylpyrrolidine[46] (Table 6, entry 13): ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.91–2.00 (m, 4H), 3.19–3.30 (m, 4H), 6.49–6.54 (m, 2H), 6.63–6.67 (m, 1H), 7.20–7.25 ppm (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=26.1, 48.1, 112.2, 115.9, 129.6, 148.5 ppm.

N,*N*-Dibutylaniline[41] (Table 6, entry 14): ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.95 (t, J=7.2 Hz, 6H), 1.35 (m, 4H), 1.50–1.61 (m, 4H), 3.24 (t, J= 7.6 Hz, 4H), 6.59–6.67 (m, 3H), 7.19 ppm (dd, J=8.8, 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=14.0, 20.4, 29.4, 50.6, 111.6, 115.0, 129.1, 148.1 ppm.

N,*N*-(Di-*n*-butyl)-*p*-toluidine[43] (Table 6, entry 15): ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.95 (t, J=7.4 Hz, 6H), 1.34 (sept, J=7.2 Hz, 4H), 1.53–1.61 (m, 4H), 2.23 (s, 3H), 3.23 (t, J=7.6 Hz, 4H), 6.57 (d, J=8.5 Hz, 2H), 7.01 ppm (d, J=8.7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=14.0, 20.2, 20.5, 29.6, 51.1, 112.5, 124.5, 129.7, 146.4 ppm.

N,*N*-Dicyclohexylaniline[49] (Table 6, entry 16): ^{1}H NMR (600 MHz, $CDCl_3$): δ=1.29–1.41 (m, 4H), 1.50–1.65 (m, 8H), 1.66–1.68 (m, 8H), 3.27–3.34 (m, 2H), 6.95–7.09 (m, 3H), 7.16–7.23 ppm (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ= 26.2, 26.6, 32.3, 57.6, 119.6, 121.5, 128.5, 149.0 ppm.

Typical Experimental Procedure for Recovery and Reuse of Catalyst in Amination (Table 7, Method A)

Iodobenzene (163.2 mg, 0.8 mmol), morpholine (139.4 mg, 1.6 mmol), **2a** (137.9 mg, 0.04 mmol, 5 mol%), and NaO*t*Bu (177.0 mg, 1.84 mmol) were combined in toluene (2.7 mL) under argon. The mixture was stirred for 5 h under reflux conditions. After the mixture was cooled to room temperature, hexane (10 mL) was added to quench the reaction, and the catalyst was collected by filtration in air, washed with hexane, and dried. The solution was evaporated to give a crude product. The volume of the residue was adjusted to 5 mL with THF to give a sample for XRF analysis for the measurement of palladium leaching. The sample solution after measurement of leaching was diluted with THF, and the yield was determined by GC analysis with naphthalene as internal standard. The recovered catalyst was washed with methanol and dried at room temperature under reduced pressure for 6 h. This recovered **2a** (130.1 mg), trichlorosilane (108.4 mg, 0.8 mmol), and triethylamine (121.4 mg, 1.2 mmol) were stirred in toluene (5.0 mL) for 24 h at 100 °C under argon to reduce the phosphine oxide moieties. The mixture was cooled to room temperature, the reaction was quenched by careful addition of methanol (5 mL), and the catalyst was washed with hexane and THF several times and dried at room temperature under reduced pressure for 12 h. This catalyst was reused several times according to the above method.

Typical Experimental Procedure for Sonogashira Coupling

Diphenylacetylene[50] (Table 8, entry 5): Iodobenzene (61.2 mg, 0.3 mmol), phenylacetylene (46.0 mg, 0.45 mmol), **2c** (28.1 mg, 0.009 mmol, 3 mol%), and cesium carbonate (147 mg, 0.45 mmol) were combined in THF (2.0 mL) under argon. The mixture was stirred for 11 h at 80 °C. After the mixture was cooled to room temperature, hexane (6 mL) was added to quench the reaction, and the catalyst was collected by filtration in air, washed with hexane and THF, and dried. The solution was evaporated to give a crude product. The volume of the residue was adjusted to 5 mL with THF to give a sample for XRF analysis for the measurement of palladium leaching. The sample solution after measurement of leaching was diluted with THF, and the yield was determined by GC analysis with naphthalene as internal standard. ^{1}H NMR (600 MHz, $CDCl_3$): δ=7.28–7.36 (m, 6H), 7.55–7.59 ppm (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=89.7, 123.7, 128.6, 128.7, 132.0 ppm.

4-Acetyldiphenylacetylene[51] (Scheme 3): The crude product was purified by PTLC (hexane/EtOAc=10:1) to give 4-acetyldiphenylacetylene (87%). ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.54 (s, 3H), 7.29–7.30 (m, 3H), 7.47–7.50 (m, 2H), 7.54 (d, J=8.6 Hz, 2H), 7.87 ppm (d, J=8.7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=26.5, 88.5, 92.6, 122.6, 128.0, 128.1, 128.3, 128.7, 131.6, 131.6, 197.1 ppm.

1-[4-(3-Hydroxy-3,3-diphenylprop-1-ynyl)phenyl]ethanone (Scheme 3): The crude product was purified by PTLC (hexane/EtOAc=4:1) to give 1-[4-(3-hydroxy-3,3-diphenylprop-1-ynyl)phenyl]ethanone (97%). ^{1}H NMR (600 MHz, $CDCl_3$): δ=2.56 (s, 3H), 7.28 (tt, J=7.6, 1.4 Hz, 2H), 7.35 (t, J=6.9 Hz, 4H), 7.55 (d, J=8.9 Hz, 2H), 7.66 (d, J=7.6 Hz, 4H), 7.88 ppm (d, J=8.9 Hz, 2H).

1-(1-Naphthyl)-2-phenylacetylene[52] (Scheme 3): The crude product was purified by PTLC (hexane) to give 1-(1-naphthyl)-2-phenylacetylene (98%). ^{1}H NMR (600 MHz, $CDCl_3$): δ=7.34–7.40 (m, 3H), 7.44 (t, J= 7.6 Hz, 1H); 7.52 (t, J=6.9 Hz, 1H), 7.58 (t, J=6.9 Hz, 1H), 7.64 (dd, J=8.2, 1.3 Hz, 2H), 7.76 (d, J=6.9 Hz, 1H), 7.84 (dd, J=15.1, 8.2 Hz, 2H), 8.44 ppm (d, J=8.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ=87.5, 94.4, 120.9, 123.4, 125.1, 126.2, 126.4, 126.7, 128.3, 128.3, 128.4, 128.8, 130.3, 131.6, 133.2, 133.2 ppm.

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